L28 ANSWER 5 OF 8 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

AB In four patients, men of 64, 66 and 69 years old and a woman of 65 years, who suffered from **chronic obstructive pulmonary disease** (**COPD**) and used inhalation corticosteroids in a relatively high dose (800-1600 .mu.g of **budesonide** per day), a pulmonary infection was diagnosed caused by Mycobacterium malmoense (the first two patients) and Aspergillus (the other two) respectively. Inhalation corticosteroids are of great importance in the treatment of asthmatic patients. Their place in the treatment of patients with **COPD** is much less clear. The patients did not have an immunological deficiency or anatomical pulmonary or bronchial deformation which could have explained the occurrence of these infections. The high dosages of inhalation corticosteroids may have been involved in the cause of these infections by suppressing the T-cell response locally. In view of this, longterm inhalation corticosteroid treatment should be prescribed in **COPD** patients only if the efficacy of the medication has been proved in the individual patient involved.

TI [Opportunistic lung infection in patients with **chronic obstructive pulmonary disease**; a side effect of inhalation corticosteroids].
OPPORTUNISTISCHE LONGINFECTIES BIJ PATIENTEN MET CHRONISCHE OBSTRUCTIEVE LONGZIEKTE; EEN BIJWERKING VAN INHALATIECORTICOSTEROIDEN?.

SO Nederlands Tijdschrift voor Geneeskunde, (**1996**) 140/2 (94-98).
ISSN: 0028-2162 CODEN: NETJAN

AB In four patients, men of 64, 66 and 69 years old and a woman of 65 years, who suffered from **chronic obstructive pulmonary disease** (**COPD**) and used inhalation corticosteroids in a relatively high dose (800-1600 .mu.g of **budesonide** per day), a pulmonary infection was diagnosed caused by Mycobacterium malmoense (the first two patients) and Aspergillus (the other two). . . Inhalation corticosteroids are of great importance in the treatment of asthmatic patients. Their place in the treatment of patients with **COPD** is much less clear. The patients did not have an immunological deficiency or anatomical pulmonary or bronchial deformation which could. . . these infections by suppressing the T-cell response locally. In view of this, longterm inhalation corticosteroid treatment should be prescribed in **COPD** patients only if the efficacy of the medication has been proved in the individual patient involved.

CT Medical Descriptors:
*chronic . . . drug therapy
*lung infection: SI, side effect
*opportunistic infection: SI, side effect
adult
aged
article
aspergillus
case report
drug efficacy
female
human
male
mycobacterium
prescription
thorax radiography
*corticosteroid: DT, drug therapy

*corticosteroid: AE, adverse drug reaction
budesonide: DT, drug therapy
formoterol: DT, drug therapy
ipratropium bromide: DT, drug therapy
prednisolone: DT, drug therapy
theophylline: DT, drug therapy

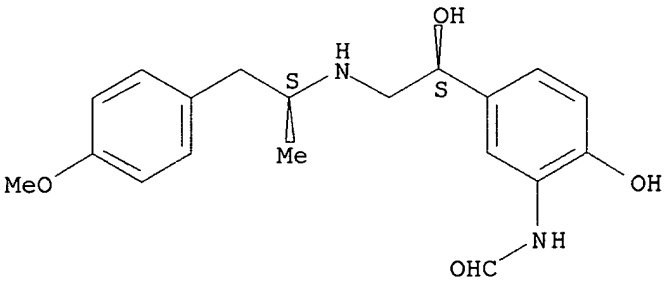
RN (**budesonide**) 51333-22-3; (**formoterol**) 73573-87-2; (ipratropium bromide) 22254-24-6; (prednisolone) 50-24-8; (theophylline) 58-55-9, 5967-84-0, 8055-07-0, 8061-56-1, 99007-19-9

L12 ANSWER 95 OF 251 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AB Respiratory muscle dysfunction has been demonstrated in several clinical situations including chronic **respiratory disease**, such as **chronic obstructive pulmonary disease**, as well as cardiac insufficiency. In the latter case, respiratory muscle dysfunction has been demonstrated in acute situation (cardiogenic shock) and in chronic cardiac insufficiency. In the former case, it has been shown in an animal model that respiratory muscle dysfunction could influence markedly the outcome of cardiogenic shock. In chronic cardiac insufficiency histologic, biochemical and contractile abnormalities of the respiratory muscles have been demonstrated in an animal model as well as in humans. These alterations may account, at least in part, for the sensation of dyspnea that these patients encountered. Finally, several pharmacological agents such as angiotensin-converting enzyme inhibitors have been shown to restore muscle abnormalities observed during chronic cardiac insufficiency.
AN 96349152 EMBASE
DN 1996349152
TI Alteration in diaphragmatic function during cardiac insufficiency: Potential pharmacology modulation.
AU Aubier M.
CS Unite de Pneumologie, Hopital Bichat, 46 rue Henri Huchard,75018 Paris, France
SO Journal of Molecular and Cellular Cardiology, (**1996**) 28/11 (2293-2302).
ISSN: 0022-2828 CODEN: JMCDAY
CY United Kingdom
DT Journal; General Review
FS 005 General Pathology and Pathological Anatomy
015 Chest Diseases, Thoracic Surgery and Tuberculosis
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LA English
SL English
TI Alteration in diaphragmatic function during cardiac insufficiency: Potential pharmacology modulation.
SO Journal of Molecular and Cellular Cardiology, (**1996**) 28/11 (2293-2302).
ISSN: 0022-2828 CODEN: JMCDAY
AB Respiratory muscle dysfunction has been demonstrated in several clinical situations including chronic **respiratory disease**, such as **chronic obstructive pulmonary disease**, as well as cardiac insufficiency. In the latter case, respiratory muscle dysfunction has been demonstrated in acute situation (cardiogenic shock). . .

=>

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 73573-87-2 REGISTRY
CN Formamide, N-[2-hydroxy-5-[(1R)-1-hydroxy-2-[[(1R)-2-(4-methoxyphenyl)-1-methylethyl]amino]ethyl]phenyl]-, rel- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Formamide, N-[2-hydroxy-5-[1-hydroxy-2-[[2-(4-methoxyphenyl)-1-methylethyl]amino]ethyl]phenyl]-, (R*,R*)-(.+-.)-
OTHER NAMES:
CN (.+-.)Formoterol
CN Eformoterol
CN Formamide, N-[2-hydroxy-5-[1-hydroxy-2-[[2-(4-methoxyphenyl)-1-methylethyl]amino]ethyl]phenyl]-, (R*,R*)-
CN **Formoterol**
CN Oxis
FS STEREOSEARCH
DR 126587-85-7, 49861-99-6, 183814-29-1
MF C19 H24 N2 O4
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CBNB, CEN, CIN, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, SYNTHLINE, TOXCENTER, TOXLIT, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

Relative stereochemistry.



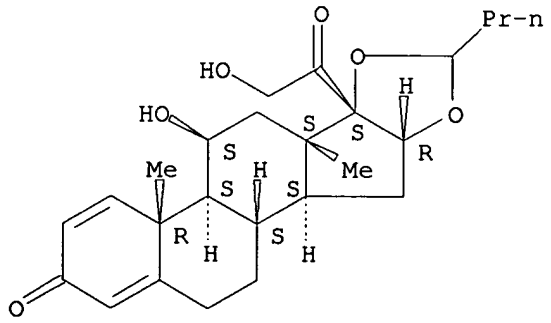
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

296 REFERENCES IN FILE CA (1967 TO DATE)
11 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
297 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=>

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 51333-22-3 REGISTRY
CN Pregna-1,4-diene-3,20-dione, 16,17-[butylidenebis(oxy)]-11,21-dihydroxy-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2H-Naphth[2',1':4,5]indeno[1,2-d][1,3]dioxole, pregna-1,4-diene-3,20-dione deriv.
OTHER NAMES:
CN 16.alpha.,17.alpha.-(Butylidenedioxy)-11.beta.,21-dihydroxypregna-1,4-diene-3,20-dione
CN **Budesonide**
CN Entocort
CN Preferid
CN Pulmicort
CN Rhinocort
CN Rhinocort Aqua
FS STEREOSEARCH
MF C25 H34 O6
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, PHAR, PHARMASEARCH, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

824 REFERENCES IN FILE CA (1967 TO DATE)
12 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
825 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> s formoterol/cn

L26 ANSWER 1 OF 3 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 95200173 EMBASE
DN 1995200173
TI Salmeterol and formoterol in partially reversible severe chronic obstructive pulmonary disease: A dose-response study.
AU Cazzola M.; Matera M.G.; Santangelo G.; Vinciguerra A.; Rossi F.; D'Amato G.
CS Div. Pneumology and Allergology, A Cardarelli Hospital,Naples, Italy
SO Respiratory Medicine, (**1995**) 89/5 (357-362).
ISSN: 0954-6111 CODEN: RMEDEY
CY United Kingdom
DT Journal; Article
FS 015 Chest Diseases, Thoracic Surgery and Tuberculosis
037 Drug Literature Index
LA English
SL English
AB When testing the response to .beta.-agonist drugs in severe **chronic obstructive pulmonary disease** (**COPD**), a dose-response assessment should be undertaken. This study compares the time course of inhaled salmeterol (25, 50 and 75 .mu.g) and **formoterol** (12, 24 and 36 .mu.g) at different doses in a group of 12 patients with partially reversible, but severe **COPD** (FEV1 of 12-32% of predicted values after .beta.-agonist drugs had been withheld for 24 h). All doses of salmeterol and **formoterol** induced a significant (P<0.01) spirometric improvement over the 12-h monitoring period, when compared to the spirometric improvement after placebo: but while **formoterol** induced a dose-dependent increase of the FVC, FEV1 and FEF50, this was not the case for salmeterol. In fact, 75 .mu.g salmeterol did not produce a further improvement of these parameters. Mean peak bronchodilation, expressed as the increase in FEV1 over baseline values, occurred 2 h after inhalation of the three doses of salmeterol, and 1 h after inhalation of the three doses of **formoterol**. A comparison of 50.mu.g salmeterol with 12 .mu.g or 24 .mu.g **formoterol** (clinically recommended doses), showed that improvement of FEV1 after salmeterol was statistically (P<0.05) higher than that after the two doses of **formoterol**, although the mean peak bronchodilations were similar. This was because salmeterol has a longer duration of action than **formoterol**. These data demonstrate that salmeterol is equally effective as, but longer-acting than, **formoterol** at clinically recommended doses in patients suffering from **COPD**, with severe airway obstruction. Moreover, these data suggest that 50 .mu.g is the best dosage for salmeterol in these patients.
CT Medical Descriptors:
*chronic obstructive lung disease: DT, drug therapy
adult
aged
article
bronchodilatation
clinical article
clinical trial
crossover procedure
dose response
drug response
forced expiratory volume
human

10/010283

inhalational drug administration
male
priority journal
randomized controlled trial
single blind procedure
spirometry
vital capacity
Drug Descriptors:
*formoterol fumarate: CT, clinical trial
*formoterol fumarate: CM, drug comparison
*formoterol fumarate: DO, drug dose
*formoterol fumarate: DT, drug therapy
*salmeterol xinafoate: CT, clinical trial
*salmeterol xinafoate: CM, drug comparison
*salmeterol xinafoate: DO, drug dose
*salmeterol xinafoate: DT, drug therapy
beta 2 adrenergic receptor stimulating agent: CT, clinical trial
beta 2 adrenergic receptor stimulating agent: DT, drug therapy
bronchodilating agent: CT, clinical trial
bronchodilating agent: DT, drug therapy
RN (formoterol fumarate) 43229-80-7; (salmeterol xinafoate) 94749-08-3
CO Glaxo (Italy); Ciba geigy (Switzerland)

L26 ANSWER 2 OF 3 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 94197516 EMBASE
DN 1994197516
TI Effect of salmeterol and formoterol in patients with chronic obstructive pulmonary disease.
AU Cazzola M.; Santangelo G.; Piccolo A.; Salzillo A.; Matera M.G.; D'Amato G.; Rossi F.
CS Via del Parco Margherita 24,80121 Napoli, Italy
SO Pulmonary Pharmacology, (**1994**) 7/2 (103-107).
ISSN: 0952-0600 CODEN: PUPHEX
CY United Kingdom
DT Journal; Article
FS 015 Chest Diseases, Thoracic Surgery and Tuberculosis
037 Drug Literature Index
LA English
SL English
AB In the present trial we investigated the time course of inhaled salmeterol and **formoterol** bronchodilation in comparison with that of inhaled salbutamol and placebo in 16 patients with moderate to severe **chronic obstructive pulmonary disease** (**COPD**). The study was performed using a single-blind crossover randomized study. The bronchodilator activity of 200 .mu.g salbutamol, 50 .mu.g salmeterol, 24 .mu.g **formoterol** and placebo, which were all inhaled from a metered dose inhaler, was investigated. Our results showed that salmeterol and **formoterol** are efficacious in reducing airflow obstruction in patients suffering from **COPD**. We found similar times of onset to improve FEV1 by 15% for salmeterol and **formoterol** (salbutamol behaving faster), while the duration of action showed the expected differences between the two long-acting drugs and salbutamol. The results indicate that long-acting .beta.2-agonists appear to be very effective in improving airway limitation in patients suffering from **COPD**. Although the onset of bronchodilation after inhaling salmeterol and **formoterol** is slightly delayed compared with salbutamol, this is of little clinical importance since in these patients salmeterol and **formoterol** must be intended for

maintenance treatment and not immediate symptomatic relief.
CT Medical Descriptors:
*chronic obstructive lung disease: DT, drug therapy
adult
aged
area under the curve
article
blood pressure
bronchodilatation
clinical article
clinical trial
controlled study
crossover procedure
drug efficacy
heart rate
human
inhalational drug administration
male
priority journal
randomized controlled trial
single blind procedure
Drug Descriptors:
*formoterol: DT, drug therapy
*formoterol: CM, drug comparison
*salbutamol: DT, drug therapy
*salbutamol: CM, drug comparison
*salmeterol: DT, drug therapy
*salmeterol: CM, drug comparison
placebo
RN (formoterol) 73573-87-2; (salbutamol) 18559-94-9; (salmeterol) 89365-50-4
CO Glaxo (Italy); Ciba geigy (Switzerland)

L26 ANSWER 3 OF 3 SCISEARCH COPYRIGHT 2002 ISI (R)
AN 95:395451 SCISEARCH
GA The Genuine Article (R) Number: RA871
TI SALMETEROL AND FORMOTEROL IN PARTIALLY REVERSIBLE SEVERE CHRONIC OBSTRUCTIVE PULMONARY-DISEASE - A DOSE-RESPONSE STUDY
AU CAZZOLA M (Reprint); MATERA M G; SANTANGELO G; VINCIGUERRA A; ROSSI F; DAMATO G
CS A CARDARELLI HOSP, DIV PNEUMOL & ALLERGOL, VIA PARCO MARGHERITA 24, I-80121 NAPLES, ITALY (Reprint); A CARDARELLI HOSP, RESP CLIN PHARMACOL UNIT, I-80121 NAPLES, ITALY; UNIV NAPLES 2, SCH MED, INST PHARMACOL & TOXICOL, NAPLES, ITALY
CYA ITALY
SO RESPIRATORY MEDICINE, (**MAY 1995**) Vol. 89, No. 5, pp. 357-362.
ISSN: 0954-6111.
DT Article; Journal
FS LIFE; CLIN
LA ENGLISH
REC Reference Count: 22
AB When testing the response to beta(2)-agonist drugs in severe **chronic obstructive pulmonary disease** (**COPD**), a dose-response assessment should be undertaken. This study compares the time course of inhaled salmeterol (25, 50 and 75 mu g) and **formoterol** (12, 24 and 36 mu g) at different doses in a group of 12 patients with partially reversible, but severe **COPD** (FEV(1) of 12-32% of predicted values after beta(2)-agonist drugs had been withheld for 24 h). All doses of salmeterol and **formoterol**

induced a significant (P<0.01) spirometric improvement over the 12-h monitoring period, when compared to the spirometric improvement after placebo, but while **formoterol** induced a dose-dependent increase of the FVC, FEV(1) and FEV(50), this was not the case for salmeterol. In fact, 75 mu g salmeterol did not produce a further improvement of these parameters. Mean peak bronchodilation, expressed as the increase in FEV(1) over baseline values, occurred 2 h after inhalation of the three doses of salmeterol, and 1 h after inhalation of the three doses of **formoterol**. A comparison of 50 mu g salmeterol with 12 mu g or 24 mu g **formoterol** (clinically recommended doses), showed that improvement of FEV(1) after salmeterol was statistically (P<0.05) higher than that after the two doses of **formoterol**, although the mean peak bronchodilations were similar. This was because salmeterol has a longer duration of action than **formoterol**. These data demonstrate that salmeterol is equally effective as, but longer-acting than, **formoterol** at clinically recommended doses in patients suffering from **COPD**, with severe airway obstruction. Moreover, these data suggest that 50 mu g is the best dosage for salmeterol in these patients.

CC CARDIOVASCULAR SYSTEM; RESPIRATORY SYSTEM

STP KeyWords Plus (R): AIR-FLOW LIMITATION; SALBUTAMOL; AGONISTS; BRONCHODILATOR; RESPONSIVENESS; THERAPY

RF 93-1664 001; REGULAR INHALED BETA-AGONIST IN ASTHMA; AIRWAY RESPONSIVENESS; PROGNOSIS OF BRONCHIAL HYPERRESPONSIVENESS

RE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)
AHRENS R C	1991	67	296	ANN ALLERGY
BARCLAY J	1982	22	389	EUR J CLIN PHARMACOL
CAZZOLA M	1994	7	103	PULM PHARMACOL
CHRYSTN H	1994	26	1	CLIN PHARM
COCHRANE G M	1984		188	BRONCHODILATOR THERA
DEROM E Y	1992	47	30	THORAX
GERMOUTY J	1992	24	342	ALLERG IMMUNOL
GUYATT G H	1987	135	1069	AM REV RESPIR DIS
GUYATT G H	1988	148	1949	ARCH INTERN MED
HARF A	1992	5	919	EUR RESPIR J
JACK D	1991	31	501	BRIT J CLIN PHARMACO
JAESCHKE R	1993	87	433	RESP MED
KOCH	1987	136	225	AM REV RESPIR DIS
KOCH G G	1972	28	577	BIOMETRICS
PRIOR J G	1982	72	266	BR J DIS CHEST
RABE K F	1993	147	1436	AM REV RESPIR DIS
SCHMITZ E	1994	48	12	PNEUMONOLOGIE
SCHULTZEWERNING.G	1993	19	355	ATEMWEG LUNGENKRANK
SCHULTZEWERNING.G	1990	168	83	LUNG
TEALE C	1991	85	281	RESP MED
TWEEDDALE P M	1987	42	487	THORAX
ULLMAN A	1988	43	674	THORAX

=>

induced a significant (P<0.01) spirometric improvement over the 12-h monitoring period, when compared to the spirometric improvement after placebo: but while **formoterol** induced a dose-dependent increase of the FVC, FEV1 and FEF50, this was not the case for salmeterol. In fact,
75. . . 2 h after inhalation of the three doses of salmeterol, and 1 h after inhalation of the three doses of **formoterol**. A comparison of 50.mu.g salmeterol with 12 .mu.g or 24 .mu.g **formoterol** (clinically recommended doses), showed that improvement of FEV1 after salmeterol was statistically (P<0.05) higher than that after the two doses
of **formoterol**, although the mean peak bronchodilations were similar. This was because salmeterol has a longer duration of action than **formoterol**. These data demonstrate that salmeterol is equally effective as, but longer-acting than, **formoterol** at clinically recommended doses in patients suffering from **COPD**, with severe airway obstruction. Moreover, these data suggest that 50 .mu.g is the best
dosage for salmeterol in these patients.

L9 ANSWER 28 OF 36 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AB In the present trial we investigated the time course of inhaled salmeterol
and **formoterol** bronchodilation in comparison with that of inhaled salbutamol and placebo in 16 patients with moderate to severe **chronic obstructive pulmonary disease** (**COPD**). The study was performed using a single-blind crossover randomized study. The bronchodilator activity of 200 .mu.g salbutamol, 50 .mu.g salmeterol, 24 .mu.g **formoterol** and placebo, which were all inhaled from a metered dose inhaler, was investigated. Our results showed that salmeterol and **formoterol** are efficacious in reducing airflow obstruction in patients suffering from **COPD**. We found similar times of onset to improve FEV1 by 15% for salmeterol and **formoterol** (salbutamol behaving faster), while the duration of action showed the expected differences between the two long-acting drugs and salbutamol. The results indicate that long-acting .beta.2-agonists appear to be very effective in improving airway limitation in patients suffering from **COPD**. Although the onset of bronchodilation after inhaling salmeterol and **formoterol** is slightly delayed compared with salbutamol, this is of little clinical importance since in these patients salmeterol and **formoterol** must be intended for maintenance treatment and not immediate symptomatic relief.
AN 94197516 EMBASE
DN 1994197516
TI Effect of salmeterol and **formoterol** in patients with **chronic obstructive pulmonary disease**
.
AU Cazzola M.; Santangelo G.; Piccolo A.; Salzillo A.; Matera M.G.; D'Amato G.; Rossi F.
CS Via del Parco Margherita 24,80121 Napoli, Italy
SO Pulmonary Pharmacology, (**1994**) 7/2 (103-107).
ISSN: 0952-0600 CODEN: PUPHEX
CY United Kingdom
DT Journal; Article
FS 015 Chest Diseases, Thoracic Surgery and Tuberculosis
037 Drug Literature Index
LA English
SL English
TI Effect of salmeterol and **formoterol** in patients with

chronic obstructive pulmonary disease
.

TI Effect of salmeterol and **formoterol** in patients with **chronic obstructive pulmonary disease**
.

SO Pulmonary Pharmacology, **(1994)** 7/2 (103-107).
ISSN: 0952-0600 CODEN: PUPHEX

AB In the present trial we investigated the time course of inhaled salmeterol and **formoterol** bronchodilation in comparison with that of inhaled salbutamol and placebo in 16 patients with moderate to severe **chronic obstructive pulmonary disease** (**COPD**). The study was performed using a single-blind crossover randomized study. The bronchodilator activity of 200 .mu.g salbutamol, 50 .mu.g salmeterol, 24 .mu.g **formoterol** and placebo, which were all inhaled from a metered dose inhaler, was investigated. Our results showed that salmeterol and **formoterol** are efficacious in reducing airflow obstruction in patients suffering from **COPD**. We found similar times of onset to improve FEV1 by 15% for salmeterol and **formoterol** (salbutamol behaving faster), while the duration of action showed the expected differences between the two long-acting drugs and salbutamol. The results indicate that long-acting .beta.2-agonists appear to be very effective in improving airway limitation in patients suffering from **COPD**. Although the onset of bronchodilation after inhaling salmeterol and **formoterol** is slightly delayed compared with salbutamol, this is of little clinical importance since in these patients salmeterol and **formoterol** must be intended for maintenance treatment and not immediate symptomatic relief.

L9 ANSWER 29 OF 36 SCISEARCH COPYRIGHT 2002 ISI (R)

AB Objective: There are several reports of documented adverse cardiac effects during treatment with beta-agonists. Since one should be aware that this may be a problem in patients with preexisting cardiac disorders, we have conducted a randomized, single-blind, balanced, crossover, placebo-controlled study to assess the cardiac effects of two single doses of **formoterol** (12 mu g and 24 mu g) and one single dose of salmeterol (50 (mu g) in 12 patients suffering from **COPD** with preexisting cardiac arrhythmias and hypoxemia (PaO2 < 60 mm Hg).

Design: Each patient was evaluated at a screening visit that included spirometry, blood gas analysis, plasma potassium measurement, and 12-lead ECG. In following nonconsecutive days, all patients underwent Holter monitoring 24 h during each of the four treatments. Holter monitoring was started soon before drug administration in the morning. Plasma potassium level was measured before drug inhalation, at 2-h intervals for 6 h, and at 9, 12, and 24 h following administration. None of our patients took rescue medication during the 24-h period.

Results: Holter monitoring showed a heart rate higher after **formoterol**, 24 mu g, than after **formoterol**, 12 mu g, and salmeterol, 50 mu g, and supraventricular or ventricular premature beats more often after **formoterol**, 24 mu g. **Formoterol**, 24 mu g, significantly reduced plasma potassium level for 9 h when compared with placebo, whereas **formoterol**, 12 mu g, was different after 2 h and salmeterol, 50 mu g, from 4 to 6 h.

Conclusions: The results of this study suggest that if a **COPD** patient is suffering from preexisting cardiac arrhythmias and hypoxemia, long-acting beta-agonists may have adverse effects on the myocardium, although the recommended single dose of salmeterol and **formoterol**